REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and remarks presented herewith, which place the application into condition for allowance, or in better condition for appeal.

Status of the Claims and Formal Matters

Claims 1-4, 13, 16-24, 26, and 27 are currently pending in this application. Claims 8-12, 14, and 25 have been withdrawn, and Claims 16 and 17 have been cancelled. Applicants reserve the right to claim withdrawn and/or cancelled subject matter in co-pending applications.

Rejections under 35 U.S.C. §103(a)

Claims 1-4, 13, 18-24, 26 and 27 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin et al, (U.S.6,610,839), "Morin" in view of Chin et al., (U.S.6,197,599), "Chin". The Office Action contends that it would have been obvious to one of skill in the art to form the immobilized proteins as described by Morin in the form of an array as taught by Chin for the advantage of identifying a protein based on its position and studying a wide variety of proteins in a single experiment for convenience. This rejection is respectfully traversed.

The present invention relates to, *inter alia*, a method of generating a protein array from a plurality of target DNA sequences. As described in the specification, "the methods of the present invention allow the specific modification, in one pot, of every member of a cDNA library in a manner which does not rely on any knowledge of the sequence of individual genes," see paragraph [0013] of the published application U.S. 20030118994.

An advantageous feature of the instant invention is that a plurality of DNA sequences can each be individually tagged with a marker moiety to facilitate the direct immobilization of the resultant tagged amino acid sequences to a solid support, which allows for purification and immobilization of the tagged amino acid sequences in a single step. This allows one of ordinary skill in the art to tag a plurality of DNA sequences and subsequently purify and immobilize the tagged expression products in a single step, via the marker tag to a solid support in a spatially

defined format. Note that all the modified amino acids (or polypeptides) are immobilized to a single solid support and purified, that is, they are all attached to the same solid support which could be a bead, microscope slide or other structure.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir.1991).

Morin relates to isolated nucleic acids that encode the catalytic subunit of human telomerase (hTRT). Specifically, Morin merely teaches that tagged hTRT sequences can be bound to a solid support to separate the fusion protein "from unbound components" (see Morin, col. 43, lines 29-34). Morin merely discloses the manipulation of a single target sequence, hTRT, and does not teach or suggest that even this single target sequence can be modified in a single reaction. Morin merely describes the manipulation of this sequence in two vectors, pPICZ B and derivative thereof. This does not constitute a "plurality of target sequences" i.e., "a library of cDNA molecules" as understood in the art.

Furthermore, Morin describes purification and immobilization of each protein species to a resin which is composed of a multitude of beads or other polymeric structures, using metal-chelate chromatography. In contrast to the present invention, the purification and immobilization as described by Morin does not relate to a single support but, in fact, to many similar supports within the resin. Notably, Morin does not teach or suggest the purification and immobilization of tagged proteins in a single step, as well as their immobilization to a solid support in a spatially-defined format.

Chin does not remedy the deficiencies of Morin. Chin does not teach or disclose methods for making a protein array by purifying and immobilizing a plurality of tagged amino acid sequences directly to a solid support via a marker tag moiety in a single step. In fact, Chin teaches away from the instantly claimed invention because Chin describes at col. 4, lines 18-26, that agents such as proteins are bound to antibodies, and the antibodies are then attached to a solid support. Chin further teaches at col. 5, lines 39-42 that "[w]hen a protein is captured by its antibody immobilized on an array, other proteins may also be tethered to the same position due to protein-protein interaction" (emphasis added), which indicates that the Chin requires proteins to be indirectly immobilized to a solid support via an antibody linker.

Chin merely relates to immobilization of proteins via protein-protein interactions with an antibody on a solid support. Furthermore, Chin requires that each individual protein be purified and immobilized separately. Taken together, Morin and Chin therefore fail to teach or suggest manipulation of a "plurality of target sequences in a single pot" and the subsequent purification and immobilization of the plurality of modified amino acids derived from the single reaction to a solid support in a single step, to create a protein array. For the foregoing reasons, it is respectfully submitted that a rejection under §103(a) by Morin in view of Chin cannot stand. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

Claims 16 and 17 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin in view of Chin, and further in view of Ben-Bassat (U.S. 4,865,974), "Ben-Bassat". In view of cancellation of claims 16 and 17, the rejection under 35 U.S.C. §103(a) is now moot. Applicants request withdrawal of the rejection.

Claim 24 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Morin in view of Chin and further in view of Orr et al., (US. 5,741,645), "Orr" and Nielsen et al., (U.S.6,350,853), "Nielson". The Office Action contends that it would have been obvious to one of skill in the art to provide two flanking markers as taught by Orr in the method taught by Morin because Orr allegedly teaches the advantage of isolating region-specific DNA markers. Further, the Office Action contends that it would have been obvious to provide the second marker immediately following a start codon as taught by Nielsen as a known location for inserting a marker. Applicants respectfully traverse this rejection.

As provided above, Applicants respectfully disagree with the rejection under §103(a), because the teachings of Morin in combination with Chin do not result with reasonable predictability in the present invention as claimed. Morin and Chin, considered alone or in combination, do not describe a method of making a protein array by tagging a plurality of target DNA sequences, and subsequently purifying and immobilizing the tagged expression products directly to a solid support via the tag moiety, in a single step and in a spatially defined format.

Orr does not cure the deficiencies of Morin and Chin. Orr merely relates to an isolated 1.2 Mb region of human chromosome 6 that contains a highly polymorphic CAG repeat region and which correlates to the spinocerebellar ataxia type 1 locus (SCA1). Orr is silent as to inserting a marker DNA sequence in frame immediately following a start codon of each of a plurality of target DNA sequences in a cDNA library, or immediately preceding a stop codon of each of the plurality of target DNA sequences to result in tagged, expressed proteins for the purpose of making a protein array. Orr merely describes the presence of naturally-occurring dinucleotide repeats that are present on either side of a large 1.2 Mb stretch of chromosome 6 that allows one of skill in the art to identify approximately where SCA1 locus is located. These naturally-occurring dinucleotide repeats are present in the chromosome and are not inserted.

Nielsen does not cure the deficiencies of Morin and Chin. Nielsen merely relates to peptide nucleic acids (PNA) having a polyamide backbone which are conjugated to lipophilic groups and are incorporated into liposomes. Nielsen does not teach or suggest inserting a marker DNA sequence in frame immediately following a start codon of each of a plurality of target DNA sequences in a cDNA library, or immediately preceding a stop codon of each of the plurality of target DNA sequences to result in tagged, expressed proteins for the purpose of making a protein array.

As provided above, Applicants respectfully disagree with the rejection under §103(a), because the teachings of Morin in combination with Chin, Orr and Nielsen do not result with reasonable predictability in the present invention as claimed. In view of the foregoing arguments, Applicants respectfully request reconsideration and withdrawal of the rejection under §103(a) over Morin in view of Chin in view of Orr and in view of Nielsen.

CONCLUSION

Favorable action on the merits is respectfully requested. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

Applicants believe no additional fees are due with the filing of this Amendment and Response; however, if any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number: **50-0311**, Customer Number: **35437**, Reference Number: **27353-501 UTIL.**

Respectfully submitted,

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